AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions of claims in the application.

Listing of Claims

1. (Currently Amended) A wound healing composition comprising isolated living cells having a wound healing phenotype, characterized ~~characterised~~ in that the cells of the composition:

(i) exhibit a 2 to 48000-fold~~, more preferably a 100 to 2000-fold,~~ higher level of expression of apolipoprotein D (ApoD) ~~than of Ribosomal protein L32 (RPL32)~~; ~~exhibit~~ a 2000 to 1600000-fold~~, more preferably a 13000 to 100000-fold,~~ higher level of expression of matrix metalloprotease 2 (MMP2) ~~than of RPL32~~; ~~exhibit~~ a 20 to 44000-fold~~, more preferably a 800 to 1800-fold,~~ higher level of expression of collagen 3a1 (Coll3a1) ~~(Coll3a11) than of RPL32~~; and ~~exhibit~~ a 20 to 150000-fold~~, more preferably a 1600 to 2500-fold,~~ higher level of expression of smooth muscle actin (SMA) ~~than of RPL32~~ relative to the expression level of Ribosomal protein L32 (RPL32); ~~and/~~or

(ii) have a banding pattern of polymerase chain reaction (PCR) products resulting from differential display identical or similar to that shown in Fig. 4 or Fig. 5 for nucleic acid expression in fibrin.

2. (Currently Amended) The wound healing composition of ~~according to~~ claim 1, in which the cells further exhibit a 1 to 500-fold~~, more preferably a 13 to 160-fold,~~ higher level of expression of "X-ray repair, complementing defective, in Chinese hamster, 1" (DD5) ~~than of RPL32~~; ~~and/or exhibit~~ a 1 to 210-fold~~, more preferably a 3 to 15-fold,~~ higher level of expression of a gene deposited as Genbank Accession No. gi | 10437022 (DD10) ~~than of RPL32~~; or ~~and/or exhibit~~ a 1 to 33-fold~~, preferably a 1 to 5-fold,~~ higher level of expression of a gene deposited as Genbank Accession No. gi | 12410897 (GB1) relative to the expression level of ~~than of~~ RPL32.

3. (Currently Amended) The wound healing composition ~~according to any preceding~~ of claim 1, in which the composition after development of the wound healing phenotype is maintained at a temperature of between about 20°C to 42°C~~, preferably about 37°C~~, and in which the cells further exhibit a 1000 to 120000-fold~~, preferably a 11000 to 53000-fold,~~ higher level of expression of ribosomal protein S24 (GB5), ~~and/~~or exhibit a 120 to 36000-fold~~, preferably a 1000 to 30000-fold,~~ higher level of expression of ribosomal protein S8 (DD12) than of RPL32, ~~and/~~or exhibit a 0 to 750000-fold~~, more preferably a 1 to 136000-fold,~~ higher level of expression of a gene deposited as Genbank Accession No. gi | 7022020 (DD2) than of RPL32.

4. (Currently Amended) The wound healing composition ~~according to any preceding~~ of claim 1, in which the composition after development of the wound healing phenotype is stored at a temperature of 2°C to 8°C~~, for example 3°C to 5°C, preferably about 4°C~~, and in which the cells further exhibit a 130 to 760-fold higher level of expression of urokinase (PLAU), ~~and/~~or exhibit a 28000 to 2065000-fold higher level of expression of vimentin (Vim) than of RPL32.

5. (Currently Amended) The wound healing composition ~~according to any preceding~~ of claim 1, in which the living cells are incubated within a protein-rich environment for up to about 14 days to allow development of the wound healing phenotype.

6. (Currently Amended) The wound healing composition of ~~according to~~ claim 5, in which the protein-rich environment comprises any of the group consisting of fibrin, collagen, fibronectin, vitronectin, alginate, agar, hyaluronic acid, modified starches, carrageenans, carob, gelatine, pectin and gelling agents.

7. (Currently Amended) The wound healing composition ~~according to either~~ of claim 5 ~~or claim 6~~, in which the protein-rich environment is a support matrix.

8. (Currently Amended) The wound healing composition of ~~according to~~ claim 7, in which the cells are suspended within the matrix, ~~preferably substantially uniformly within the matrix~~.

9. (Currently Amended) The wound healing composition ~~according to either~~ of claim 7 ~~or claim 8~~, in which the matrix is protein-based~~, for example having a protein concentration in the range of about 3 to 12 mg.ml^{-1}~~.

10. (Currently Amended) The wound healing composition of claim 7 ~~according to any of claims 7 to 9~~, in which the matrix is a fibrin matrix.

11. (Currently Amended) The wound healing composition of ~~according to~~ claim 10, in which the fibrin has a concentration in the range of 3 to 12 mg.ml^{-1}~~, for example 7 to 12 mg.ml^{-1} or 3 to 5 mg.ml^{-1}~~.

12. (Currently Amended) The wound healing composition ~~according to either~~ of claim 10 ~~or claim 11~~, in which the fibrin matrix is formed by thrombin-mediated polymerisation of fibrinogen.

13. (Currently Amended) The wound healing composition of claim 7 ~~according to any of claims 7 to 12~~, in which the matrix is non-pyrogenic and/or sterile.

14. (Currently Amended) The wound healing composition of claim 7 ~~according to any of claims 7 to 13~~, in which the cells are cast into the support matrix before incubation.

15. (Currently Amended) The wound healing composition of claim 7 ~~according to any of claims 7 to 14~~, in which the matrix is solid or semi-solid.

16. (Currently Amended) The wound healing composition of claim 1 ~~according to any preceding claim~~, in which the composition is stored for up to about 40 days~~, preferably up to 19 days and more preferably about 7 to 14 days or about 7 to 11 days~~ at a temperature of 2°C to 8°C~~, for example 3°C to 5°C, preferably about 4°C,~~ while retaining the wound healing phenotype.

17. (Currently Amended) The wound healing composition of claim 1 ~~according to any preceding claim~~, in which the cells are mammalian~~, for example human~~.

18. (Currently Amended) The wound healing composition of claim 1 ~~according to any preceding claim~~, in which the cells are substantially fibroblasts~~, for example 90% to 100%, preferably 95% to 99.5%, and more preferably 97.5% to 99% fibroblasts~~.

19. (Currently Amended) The wound healing composition of ~~according to~~ claim 18, in which the fibroblasts are dermal fibroblasts~~, preferably human dermal fibroblasts~~.

20. (Currently Amended) The wound healing composition of claim 1 ~~according to any preceding claim~~, in which the cells substantially exclude keratinocytes.

21. (Currently Amended) The wound healing composition of claim 1 ~~according to any preceding claim~~, in which the cells are human dermal fibroblasts within a sterile, non-pyrogenic support matrix formed by thrombin-mediated polymerisation of fibrinogen, and in which the composition has been incubated for 16 to 24 h at about 37°C.

22-54 (Cancelled)

55. (New) The wound healing composition of claim 1, in which the cells exhibit a 100 to 2000-fold higher level of expression of ApoD; a 13000 to 100000-fold higher level of expression of MMP2; a 800 to 1800-fold higher level of expression of Coll3a1; or a 1600 to 2500-fold higher level of expression of SMA relative to the level of expression of RPL32.

56. (New) The wound healing composition of claim 2, in which the cells further exhibit a 13 to 160-fold higher level of expression of DD5; a 3 to 15-fold higher level of expression of DD10; or a 1 to 5-fold higher level of expression of GB1 relative to the level of expression of RPL32.

57. (New) The wound healing composition of claim 3, in which the composition is maintained at a temperature of about 37°C, or in which the cells further exhibit a 11000 to 53000-fold higher level of expression of GB5, a 1000 to 30000-fold higher level of expression of DD12 , or a 1 to 136000-fold higher level of expression of DD2 relative to the level of expression of RPL32.

58. (New) The wound healing composition of claim 8, in which the cells are suspended substantially uniformly within the matrix.

59. (New) The wound healing composition of claim 9, in which the matrix has a protein concentration in the range of about 3 to 12 $mg.ml^{-1}$.

60. (New) The wound healing composition of claim 11, in which the fibrin has a

concentration in the range of 7 to 12 $mg.ml^{-1}$ or 3 to 5 $mg.ml^{-1}$.

61. (New) The wound healing composition of claim 16, in which the composition is stored for up to about 19 days.

62. (New) The wound healing composition of claim 61, in which the composition is stored for up to about 7 to 14 days or about 7 to 11 days.

63. (New) The wound healing composition of claim 17, in which the cells are human.

64. (New) The wound healing composition of claim 18, in which fibroblasts comprise between about 90% to 100% of the cells of said composition.

65. (New) The wound healing composition of claim 19, in which the fibroblasts are human dermal fibroblasts.

66. (New) The wound healing composition of claim 1, in which the composition is incubated for up to about 8 days to allow development of the wound healing phenotype.

67. (New) The wound healing composition of claim 66, in which the composition is incubated for up to about 96 h, 72 h, 48 h, 25 h, or 24 h to allow development of the wound healing phenotype.

68. (New) The wound healing composition of claim 66, in which the composition is incubated for up to about 16 h to 24 h to allow development of the wound healing phenotype.

69. (New) The wound healing composition of claim 1, in which the composition is incubated at a temperature of about 37°C to allow development of the wound healing phenotype.

70. (New) The wound healing composition of claim 1, in which the cells are actively synthetic or able to become actively synthetic rapidly.

71. (New) The wound healing composition of claim 1, in which the cells are not proliferating or not senescent.

72. (New) The wound healing composition of claim 1, further comprising a protease inhibitor.

73. (New) The wound healing composition of claim 72, in which the protease inhibitor is aprotinin or tranexamic acid.

74. (New) The wound healing composition of claim 1, in which the composition has a thickness of approximately 8 mm or less.

75. (New) The wound healing composition of claim 74, in which the composition has a thickness of approximately 5 mm or less.

76. (New) The wound healing composition of claim 1, comprising about 450 to 2500 cells per mm^2.

77. (New) The wound healing composition of claim 1, in which the composition

is single-layered.

78. (New) The wound healing composition of claim 1, in which the composition is packaged in a container suitable for transporting the composition, storing the composition, or topically applying the composition to a skin surface.

79. (New) The wound healing composition of claim 78, in which the container comprises a flexible pouch consisting of two sheets of impermeable flexible material peripherally sealed to provide a means of containment for the composition, the pouch comprising a first internal surface to which the composition is adherent at a level of adhesion more than between the composition and a second internal surface of the pouch but less than that between the composition and the skin surface, such that in use the pouch may be opened by parting the sheets and the composition conveniently manipulated and directly applied to the skin surface without further requirement for the composition to be touched directly by any other means prior to application.

80. (New) The wound healing composition of claim 78, in which the container is an Oliver (RTM) Products Company "Solvent Resistant Peelable Pouching Material" (Product number Q15/48BF1).

81. (New) The wound healing composition of claim 1, for use as a medicament.

82. (New) The wound healing composition of claim 1, for use as a medicament in the treatment of a skin lesion.

83. (New) The wound healing composition of claim 81, wherein said medicament is used for topical application to a skin lesion.

84. (New) The wound healing composition of claim 83, wherein said skin lesion is a venous ulcer, diabetic ulcer, pressure sore, burn or iatrogenic grating wound.

85. (New) A wound healing composition comprising fibroblasts cultured within a fibrin matrix, in which the fibroblasts of the composition have a wound healing phenotype and have a higher level of expression of collagen 6al (Coll6a), apolipoprotein D (APOD), collagen 3a1 (Coll3al), ribosomal protein L32 (RPL32), plasminogen activator inhibitor (PAI), urinary plasminogen activator (PLAU), vimentin (Vim), smooth muscle actin (SMA) and cyclo-oxygenase 2 (Cox2) than fibroblasts cultured in a collagen matrix and fibroblasts cultured in medium without a matrix.

86. (New) The wound healing composition of claim 85, in which the fibroblasts of the composition have approximately a 3-fold higher level of expression of Coll6a, an 8-fold higher level of expression of APOD, an 80-fold higher level of expression of Coll3al, a 3-fold higher level of expression of RPL32, a 3-fold higher level of expression of PAI, a 20-fold higher level of expression of PLAU, a 20-fold higher level of expression of Vim, a 5-fold higher level of expression of SMA, or an 8000-fold higher level of expression of Cox2, than fibroblasts cultured in a collagen matrix.

87. (New) The wound healing composition of claim 85, in which the fibroblasts of the composition have approximately a 4-fold higher level of expression of Coll6a, a 4-fold higher level of expression of APOD, a 10-fold higher level of expression of Coll3al, a 2-fold higher level of expression of RPL32, a 3-fold higher level of expression of PAI, a 30-fold higher level of expression of PLAU, a 10-fold higher level of expression of Vim, a 2-fold higher level of expression of SMA, or a 5000-fold higher level of expression of Cox2, than fibroblasts cultured in medium without a matrix

88. (New) The wound healing composition of claim 85, in which the fibroblasts of the composition have a higher level of expression of matrix metalloprotease 2 (MMP2), insulin induced gene I (INSIG1), growth arrest specific gene 6 (Gas6) and collagen 1al (Coll1a) than fibroblasts cultured in a collagen matrix.

89. (New) The wound healing composition of claim 88, in which the fibroblasts of the composition have approximately a 2-fold higher level of expression of MMP2, INSIG1, Gas6 or Coll1a than fibroblasts cultured in a collagen matrix.

90. (New) The wound healing composition of claim 85, in which the fibroblasts of the composition have a higher level of expression of glyceraldehydes-3-phosphate dehydrogenase (GAPDH) than fibroblasts cultured in medium without a matrix.

91. (New) The wound healing composition of claim 90, in which the fibroblasts of the composition have approximately a 3-fold higher level of expression of GAPDH than fibroblasts cultured in medium without a matrix.

92. (New) The wound healing composition of claim 85, in which the composition is incubated for up to about 8 days to allow development of the wound healing phenotype.

93. (New) The wound healing composition of claim 92, in which the composition is incubated for up to about 96 h, 72 h, 48 h, 25 h, or 24 h to allow development of the wound healing phenotype.

94. (New) The wound healing composition of claim 92, in which the composition is incubated for up to about 16 h to 24 h to allow development of the wound healing

phenotype.

95. (New) The wound healing composition of claim 85, in which the composition is incubated at a temperature of about 37°C to allow development of the wound healing phenotype.

96. (New) The wound healing composition of claim 85, in which the cells are actively synthetic or able to become actively synthetic rapidly.

97. (New) The wound healing composition of claim 85, in which the cells are not proliferating or not senescent.

98. (New) The wound healing composition of claim 85, further comprising a protease inhibitor.

99. (New) The wound healing composition of claim 98, wherein said protease inhibitor is aprotinin or tranexamic acid.

100. (New) The wound healing composition of claim 85, in which the composition has a thickness of approximately 8 mm or less.

101. (New) The wound healing composition of claim 100, in which the composition has a thickness of approximately 5 mm or less.

102. (New) The wound healing composition of claim 85, comprising about 450 to 2500 cells per mm^2.

103. (New) The wound healing composition of claim 85, in which the composition is single-layered.

104. (New) The wound healing composition of claim 85, in which the composition is packaged in a container suitable for transporting the composition, storing the composition, or topically applying the composition to a skin surface.

105. (New) The wound healing composition of claim 104, in which the container comprises a flexible pouch consisting of two sheets of impermeable flexible material peripherally sealed to provide a means of containment for the composition, the pouch comprising a first internal surface to which the composition is adherent at a level of adhesion more than between the composition and a second internal surface of the pouch but less than that between the composition and the skin surface, such that in use the pouch may be opened by parting the sheets and the composition conveniently manipulated and directly applied to the skin surface without further requirement for the composition to be touched directly by any other means prior to application.

106. (New) The wound healing composition of claim 104, in which the container is an Oliver (RTM) Products Company "Solvent Resistant Peelable Pouching Material" (Product number Q15/48BF1).

107. (New) The wound healing composition of claim 85, for use as a medicament.

108. (New) The wound healing composition of claim 85, for use as a medicament in the treatment of a skin lesion.

109. (New) The wound healing composition of claim 107, wherein said medicament is used for topical application to a skin lesion.

110. (New) The wound healing composition of claim 109, wherein said skin lesion is a venous ulcer, diabetic ulcer, pressure sore, burn or iatrogenic grating wound.

111. (New) A method of manufacturing a wound healing composition, wherein said wound healing composition comprises:

(a) isolated living cells having a wound healing phenotype, characterized in that the cells of the composition:

(i) exhibit a 2 to 48000-fold higher level of expression of apolipoprotein D (ApoD); a 2000 to 1600000-fold higher level of expression of matrix metalloprotease 2 (MMP2); a 20 to 44000-fold higher level of expression of collagen 3a1 (Coll3a1); and a 20 to 150000-fold higher level of expression of smooth muscle actin (SMA) relative to the expression level of Ribosomal protein L32 (RPL32); or

(ii) have a banding pattern of polymerase chain reaction (PCR) products resulting from differential display identical or similar to that shown in Fig. 4 or Fig. 5 for nucleic acid expression in fibrin; or

(b) fibroblasts cultured within a fibrin matrix, in which the fibroblasts of the composition have a wound healing phenotype and have a higher level of expression of collagen 6a1 (Coll6a), apolipoprotein D (APOD), collagen 3a1 (Coll3al), ribosomal protein L32 (RPL32), plasminogen activator inhibitor (PAI), urinary plasminogen activator (PLAU), vimentin (Vim), smooth muscle actin (SMA) and cyclo-oxygenase 2 (Cox2) than fibroblasts cultured in a collagen matrix and fibroblasts cultured in medium without a matrix;

said method comprising the steps of:

suspending the living cells or fibroblasts in a protein-rich environment; and

incubating the living cells or fibroblasts under conditions which allow development of a wound healing phenotype in the living cells or fibroblasts, thereby forming the wound healing composition.

112. (New) The method of claim 111, in which the living cells or fibroblasts are suspended in a solution comprising a polymerisation agent or a monomer capable of being polymerised by the polymerisation agent into a matrix, and in which the method comprises a further step of forming a single-layered support matrix comprising the living cells or fibroblasts by polymerisation of the monomer with the polymerisation agent prior to incubating the living cells or fibroblasts.

113. (New) The method of claim 112, in which the matrix is formed by adding monomer or polymerisation agent to the solution such that both monomer and polymerisation agent are present in sufficient concentrations to effect polymerisation.

114. (New) The method of claim 112, in which the monomer is fibrinogen and the polymerisation agent is thrombin.

115. (New) The method of claim 112, in which polymerization occurs in a mold.

116. (New) The method of claim 111, comprising the further step of packaging the wound healing composition into a container for storing the composition, transporting the composition, or for topically applying the composition to a skin surface of a patient.

117. (New) A method of manufacturing a wound healing composition, wherein said wound healing composition comprises:

(a) isolated living cells having a wound healing phenotype, characterized in that the

cells of the composition:

(i) exhibit a 2 to 48000-fold higher level of expression of apolipoprotein D (ApoD); a 2000 to 1600000-fold higher level of expression of matrix metalloprotease 2 (MMP2); a 20 to 44000-fold higher level of expression of collagen 3a1 (Coll3a1); and a 20 to 150000-fold higher level of expression of smooth muscle actin (SMA) relative to the expression level of Ribosomal protein L32 (RPL32); or

(ii) have a banding pattern of polymerase chain reaction (PCR) products resulting from differential display identical or similar to that shown in Fig. 4 or Fig. 5 for nucleic acid expression in fibrin; or

(b) fibroblasts cultured within a fibrin matrix, in which the fibroblasts of the composition have a wound healing phenotype and have a higher level of expression of collagen 6al (Coll6a), apolipoprotein D (APOD), collagen 3a1 (Coll3al), ribosomal protein L32 (RPL32), plasminogen activator inhibitor (PAI), urinary plasminogen activator (PLAU), vimentin (Vim), smooth muscle actin (SMA) and cyclo-oxygenase 2 (Cox2) than fibroblasts cultured in a collagen matrix and fibroblasts cultured in medium without a matrix;

said method comprising the steps of forming a single-layered support matrix by polymerising a polymerisable monomer with a polymerisation agent, casting the living cells or fibroblasts into the support matrix, and incubating the matrix under conditions which allow development of a wound healing phenotype in the living cells or fibroblasts, thereby forming the wound healing phenotype.

118. (New) The method of claim 117, in which the monomer is fibrinogen and the polymerisation agent is thrombin.

119. (New) The method of claim 117, in which polymerization occurs in a mold.

120. (New) The method of claim 117, comprising the further step of packaging the wound healing composition into a container for storing the composition, transporting the composition, or for topically applying the composition to a skin surface of a patient.

121. (New) Use of living cells as defined in claim 1 in the manufacture of a wound healing composition for the treatment of a skin lesion.

122. (New) A method for treating a skin lesion comprising topically applying the wound healing composition of claim 1 to said skin lesion.

123. (New) Use of living cells as defined in claim 85 in the manufacture of a wound healing composition for the treatment of a skin lesion.

124. (New) A method of treating a patient suffering from a skin lesion comprising topically applying of the wound healing composition of claim 85 to the skin lesion.

125. (New) A method of determining whether a composition comprising living cells has a wound healing phenotype, comprising the steps of:

(i) quantifying the cellular expression level of one or more of the following genes: apolipoprotein D (ApoD), matrix metalloprotease 2 (MMP2), collagen 3a1 (Coll3a1), smooth muscle actin (SMA), "X-ray repair, complementing defective, in Chinese hamster, 1" (DD5), a gene deposited as Genbank Accession No. gi | 10437022 (DD10), a gene deposited as Genbank Accession No. gi | 12410897 (GB1), ribosomal protein S24 (GB5), ribosomal protein S8 (DD12), a gene deposited as Genbank Accession No. gi | 7022020 (DD2), urokinase (PLAU), and vimentin (Vim) in the cells of the composition; and

(ii) comparing the expression level of the genes to the expression level of Ribosomal protein L32 (RPL32), wherein a higher expression level of the genes relative to RPL32 indicates the composition has a wound healing phenotype.

126. (New) A method of determining whether a composition comprising living fibroblast cells within a fibrin matrix has a wound healing phenotype, comprising the steps of:

(i) quantifying the expression level of one or more of the following genes: collagen 6a1 (Coll6a), apolipoprotein D (APOD), collagen 3a1 (Coll3a1), ribosomal protein L32 (RPL32), plasminogen activator inhibitor (PAI), urinary plasminogen activator (PLAU), vimentin (Vim), smooth muscle actin (SMA), cyclo-oxygenase 2 (Cox2), matrix metalloprotease 2 (MMP2), insulin induced gene I (INSIG1), growth arrest specific gene 6 (Gas6), collagen 1a1 (Coll1a), and glyceraldehydes-3-phosphate dehydrogenase (GAPDH) in the cells of the composition; and

(ii) comparing the expression level of the genes in the composition to the expression level of the genes in fibroblasts cultured in a collagen matrix and in fibroblasts cultured in medium without a matrix, wherein a higher expression level of the genes in the cells of the composition indicates the composition has a wound healing phenotype.

127. (New) A method for conducting a business, comprising the step of determining whether a composition has a wound healing phenotype according to the method of claim 125.

128. (New) A method for conducting a business, comprising the step of determining whether a composition has a wound healing phenotype according to the method of claim 126.